

# GSTO AND AS3MT GENE POLYMORPHISMS AND DIFFERENCES IN URINARY ARSENIC CONCENTRATIONS AMONG RESIDENTS IN BANGLADESH

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**Background and Aims:** The main objective of this paper is to determine whether single nucleotide polymorphisms (SNPs) in the glutathione S-transferase omega (*GSTO*) and arsenic(III)methyltransferase (*AS3MT*) genes are associated with the concentrations of urinary arsenic among individuals without arsenic-induced skin lesions.

**Methods:** A case-control study (N=900 cases; 900 controls) was conducted in rural Bangladesh to investigate the environmental and genetic risk factors associated with skin lesions. This analysis was limited to the controls in order to eliminate any possible confounding by disease status. Water and urine samples were collected and analyzed for arsenic concentrations using inductively coupled plasma-mass spectrometry (ICP-MS), and the following SNPs were detected in DNA extracted from whole blood: *GSTO1* rs4925, *GSTO2* rs156697, *GSTO2* rs2297235, and *AS3MT* rs11191439. The arsenic species measured in urine included arsenite ( $\text{As}^{\text{V}}$ ), arsenate ( $\text{As}^{\text{III}}$ ), monomethylarsonic acid (MMA), and dimethylarsinic acid (DMA). We performed linear regression for each urinary metabolite using the dominant genetic model while controlling for water arsenic levels, age, sex, body mass index (BMI), education, and urinary creatinine levels. Additionally, a pathway analysis was used to simultaneously evaluate the associations among drinking water arsenic levels, urinary arsenic metabolites and SNPs in the *GSTO* and *AS3MT* genes using PROC CALIS in SAS.

**Results:** The variant genotype in the *GSTO* genes were associated with lower urinary arsenic concentrations, specifically MMA, DMA, and total As, indicating an overall decrease in urinary arsenic excretion. Conversely, the variant genotype, Met287Thr, in the *AS3MT* gene had higher urinary arsenic concentrations, specifically  $\text{As}^{\text{III}}$  and MMA, compared to the wild type.

**Conclusions:** Among healthy individuals, genetic polymorphisms in the glutathione-s transferase omega genes and arsenic methyltransferase genes potentially modify arsenic metabolism as evidenced by altered urinary arsenic excretion. The linear regression models and pathway analysis resulted in similar findings.